ticholinergic compounds appear to be more effective bronchodilators than β-agonists. In chronic obstructive pulmonary disease, therefore, ipratropium eventually may be considered a first-line bronchodilator agent, possibly in combination with theophylline, a β-agonist or both.

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Clinical Utility of Bronchoalveolar Lavage

BRONCHOALVEOLAR LAVAGE (BAL) is a powerful addition to the repertoire of fiber-optic bronchoscopy techniques. In contrast to traditional "bronchial washing," which obtains specimens only from the proximal airways, BAL allows direct sampling of alveolar contents by simple irrigation of the lung with a bronchoscope wedged in a segmental or subsegmental bronchus. As a clinical diagnostic tool, it has proved far more useful than initially suspected. Its greatest success has come in the diagnosis of pulmonary infiltrates in the setting of immunocompromised patients, especially those with the acquired immunodeficiency syndrome. It has proved nearly 100% effective in the diagnosis of *Pneumocystis carinii* pneumonia, a primarily alveolar infection, and has been quite helpful in diagnosing other infections as well, such as *Mycobacterium avium*-intracellulare and cytomegalovirus. There are scattered reports of its efficacy in the diagnosis of noninfectious problems as well—such as adenocarcinoma, pulmonary hemorrhage, asbestosis and alveolar proteinosis. Therefore, though its sensitivity and specificity have not been completely elucidated, BAL is currently indicated in any patient undergoing fiber-optic bronchoscopy for an undiagnosed mass or infiltrate. It will add substantially to the yield of traditional bronchoscopic techniques—that is, bronchial brushing and transbronchial biopsy—with almost no increase in time, expense or morbidity of the procedure.

Bronchoalveolar lavage was initially described for clinical use in the staging of disease activity in patients with interstitial lung diseases. Comparison between specimens from lavage and histologic specimens from simultaneous open-lung biopsy has shown remarkably good correlation in the distribution of cell types—cell differential—between the two procedures. BAL also allows recovery of specific lung proteins such as fibronectin, collagenase and leukotrienes that may provide insight into pathogenetic mechanisms of a variety of diseases, especially asthma and the interstitial lung diseases (sarcoidosis, chronic hypersensitivity pneumonitis and idiopathic pulmonary fibrosis). Patients with active inflammation in the lung due to idiopathic pulmonary fibrosis were reported to have an increased percentage of polymorphonuclear leukocytes in their lavage fluid, whereas those with sarcoidosis or chronic hypersensitivity pneumonitis were said to have increased lymphocytes. Unfortunately, this simple separation of disease types by cell differentials has not proved satisfactory. There is considerable variability in the determination of simple cell differentials among different laboratories. Furthermore, the findings on cell differentials have not proved reliable for predicting either disease activity or responsiveness to therapy, and more reliable markers of disease activity are not yet available. Therefore, as far as the staging of interstitial lung disease is concerned, at the present time BAL should be regarded as strictly a research tool with great promise for the future.

Except for transient low-grade fever, modest hypoxemia and patchy pulmonary infiltrates in the area of lavage, the procedure has proved itself remarkably free of serious complications. It can even be done in patients with bleeding diatheses or those being maintained on mechanical ventilation.

In sum, BAL is a surprisingly safe technique that has become a routine part of fiber-optic bronchoscopy carried out for the diagnosis of unexplained pulmonary infiltrates or masses. Its role in the staging of interstitial lung diseases remains to be established but it has already proved itself as a valuable research tool in studying lung inflammation.

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Sarcoidosis and Hypercalcemia

HYPERCALCEMIA AND HYPERCALCIURIA are frequent complications of sarcoidosis. The estimated incidence of hypercalcemia is about 11%; hypercalciuria, however, is three times more common. These abnormalities of calcium metabolism are due to increased production of calcitriol or 1,25-dihydroxyvitamin D_3 (1,25-[OH] 2-D_3). Serum levels of calcitriol, the active metabolite of vitamin D, are increased in patients with sarcoidosis who have either hypercalcemia or hypercalciuria or both.

In healthy nonpregnant humans, vitamin D is converted by the liver to 25-hydroxyvitamin D, which in turn undergoes hydroxylation in the kidney to form 1,25-hydroxyvitamin D_3 (calcitriol). The production of 1,25-dihydroxyvitamin D_3 is tightly regulated by parathyroid hormone. In patients with sarcoidosis, uncontrolled production of 1,25-dihydroxyvitamin D_3 occurs at extrarenal sites, namely, blood monocytes, alveolar macrophages and tissue granulomas. These patients are unusually sensitive to vitamin D, which in small doses can produce hypercalcemia. The availability of more precursor vitamin D (diet, medicine, sunlight) leads to increased 1,25-dihydroxyvitamin D_3, which in turn promotes intestinal absorption of calcium.